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APPLICATION NUMBER	FILING DATE	FIRST NAM...	...ED APPLICANT	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	11

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 4/14/97.

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-21, 25-36 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-21, 25-36 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ ...otice of Draftsperson's Patent Drawing Review, PTO-948

☐ ...f Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

★ U.S. GPO: 1996-410-238/40050

The amendment filed April 14, 1997 has been entered.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the invention, as previously stated (paper 8, p. 2).

The specification does not teach how to use the methods of claims 2-6, which recite that the rate of transcription of a gene is increased. Applicants apparently intended to remove this language from all of the claims, but overlooked claims 2-6. Even if the claims were amended to remove this language, claims 3, 4 and 6 would still be enabled only for methods utilizing the TNFα gene for the reasons discussed below.

Claims 1, 7-30 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for methods and compositions utilizing the TNFα gene, as previously stated (paper 8, p. 4). Applicants argue that many of the claims do not recite "cytokines." While correct, this argument is not persuasive because these claims recite "a radiosensitizing polypeptide" which is even broader than "cytokines." While it may not require undue experimentation to test other agents *in vitro*, the claims all encompass *in vivo* methods. The effect of expressing other polypeptides, such as cytokines, is unpredictable for the reasons discussed in the previous action. Therefore it would require undue experimentation to practice the full scope of the claimed invention.

Claims 1-11, 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 remains incomplete because it lacks a step wherein the gene is expressed.

Claim 1 is indefinite in its recitation of "said cell," which lacks antecedent basis.

Claim 4 is indefinite in its recitation of "increasing the transcription," which lacks antecedent basis.

Claims 4, 7 and 15 are improper dependent claims because they do not further limit claim 1, unless "providing" a gene to a cell is somehow different from transfection. The specification does not appear to disclose any other method for "providing" besides transfection.

Claims 5, 16 and 17 are essentially duplicates of claims 2, 3 and 6, respectively, unless providing is different from transfecting, as discussed above.

Claims 7 and 15 are identical in scope because claim 1 recites that the gene is linked to the promoter.

With regard to claims which are duplicate in scope, Applicants are reminded that if one claim were to be allowed, the other would be subject to a rejection for double patenting. See MPEP 706.03(k).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 15-18, 29, 31, 33, 35 and 36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. (C15) in view of Teng et al. (C33), Neta et al. (C21) and Vile et al., as previously stated (paper 8, pp. 6-8).

Claims 8, 9, 19 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al., Neta et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31, 33, 35 and 36 above, and further in view of Felgner et al., as previously stated (paper 8, p. 8).

Claims 8, 10, 12-14, 19, 21, 25-28, 30 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al., Neta et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31, 33, 35 and 36 above, and further in view of Herz et al. (C18), as previously stated (paper 8, p. 9).

Claims 8, 11, 19, 30 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al., Neta et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31, 33, 35 and 36 above, and further in view of Breakefield et al., as previously stated (paper 8, pp. 9-10).

Claim 34 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al., Neta et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31, 33, 35 and 36 above, and further in view of Mattern et al., as previously stated (paper 8, p. 10).

Claims 1-7, 15-18, 29, 31 and 33-35 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan (C16) in view of Teng et al. and Vile et al., as previously stated (paper 8, pp. 10-11).

Claims 8, 9, 19 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31 and 33-35 above, and further in view of Felgner et al., as previously stated (paper 8, pp. 11-12).

Claims 8, 10, 12-14, 19, 21, 25-28, 30 and 32 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hallahan et al. in view of Teng et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31 and 33-35 above, and further in view of Herz et al., as previously stated (paper 8, pp. 12-13).

Claims 8, 11, 19, 30 and 32 are rejected under 35 U.S.C. § 103 as being unpatentable over Hallahan et al. in view of Teng et al. and Vile et al. as applied to claims 1-7, 15-18, 29, 31 and 33-35 above, and further in view of Breakefield et al., as previously stated (paper 8, p. 13).

Applicants traverse the above 9 rejections on the same grounds, so they will be treated together. Applicants argue that one can not predict the effect of expressing TNF endogenously from experiments wherein TNF is supplied exogenously. This argument is not persuasive because Teng et al. utilized cells which were transfected with a TNF gene, then implanted *in vivo*. Furthermore, the TNF effect was found

to be dependent on its secretion, since anti-TNF antibodies inhibited the effect (see abstract, e.g.). Once the TNF is secreted, it would be expected to have the same effect as exogenously supplied TNF.

Applicants argue that the prior art must provide a suggestion to make the claimed invention and evidence suggesting that the invention would be successful. These arguments are not persuasive. Both Hallahan et al. references suggest combining TNF treatment with radiation *in vivo*, and one specifically suggests beginning clinical trials of the claimed gene therapy method. The references provide abundant evidence suggesting that the claimed invention would be successful, as detailed in the previous Office action. Applicants' argument to the contrary is not persuasive absent any explanation of how the prior art is deficient.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce Campell, whose telephone number is 703-308-4205. The examiner can normally be reached on Monday-Thursday from 8:30 to 5:00 (Eastern time). The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on 703-308-2035. The FAX phone number for art unit 1819 is 703-308-0294.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Bruce Campell
July 2, 1997

Bruce Campell

UCE R. CAMPELL
MARY EXAMINER
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